REMARKS/ARGUMENTS

Upon entry of the present amendment, claims 1-19 will be pending in this application and presented for examination. Claims 8, 10 and 19 have been amended to explicitly recite the compounds set forth in Table 1. As such, Applicants submit that no new matter has been introduced with the foregoing amendments. Reconsideration is respectfully requested.

I. FORMALITIES

Applicants appreciate the Examiner's acknowledgment that the telephone restriction requirement has been withdrawn. In response to a mailed election of species requirement (mailed on December 14, 2004), Applicants elected a disclosed species of the invention (the compound set forth in Example 117) to comply with the requirements of 35 U.S.C § 121. In this Office Action, the Examiner stated that compounds and methods wherein W is a member of the first three groups shown in the definition of W in claim 1, wherein X is furanylene or furyl, R^6 is furyl or phenyl; and wherein the compounds are not further heterocyclic, cyano, sulfonamide, ester, carbamate or acid containing were examined on their merits, and that "claims 5-7 and all other compounds and methods are withdrawn." (Office Action, pg. 2.) Applicants respectfully traverse the withdrawal from consideration of this subject matter. The species election was made merely for search purposes under MPEP § 803.02, and in no way limits the scope of the invention to the elected species. As the Examiner is aware, proper restriction practice is set forth in MPEP § 803.02 which states:

> [a]s an example, in the case of an application with a Markush-type claim drawn to the compound C-R, wherein R is a radical selected from the group consisting of A, B, C, D, and E, the examiner may require a provisional election of a single species, CA, CB, CC, CD, or CE. The Markush-type claim would then be examined fully with respect to the elected species and any species considered to be clearly unpatentable over the elected species...[S]hould no prior art be found that anticipates or renders obvious the elected species, the **search of the Markush-type claim will be extended**. If prior art is then found that anticipates or renders obvious the Markush-type claim with respect to a nonelected species, the Markush-type claim shall be rejected and claims to the nonelected species held withdrawn from further consideration. (Emphasis added)

As the remarks and amendments herein place the examined subject matter in condition for allowance, Applicants are now entitled to a full search and examination of the entire claim scope.

II. THE INVENTION

The present invention provides for compounds, compositions and methods of selective inhibitors of cathepsin S over other isozymes in the cathepsin family, *e.g.*, cathepsin K. The methods relate to using these compounds for the treatment of disease states that would benefit from the selective inhibition of cathepsin S over other cathepsin isozymes.

III. OBVIOUSNESS-TYPE DOUBLE PATENTING REJECTION

The Examiner has rejected claims 1-4 and 8-19 under the judicially created obviousness-type double patenting as allegedly being obvious over the claims of co-pending U.S. Application No. 10/807,613. In response, Applicants respectfully request that this rejection be held in abeyance until such time when the claims in the instant application are deemed otherwise allowable. Applicants will thereafter file a terminal disclaimer in accordance with 37 CFR §1.321 to obviate the obviousness-type double patenting rejection.

IV. REJECTION UNDER 35 U.S.C. § 112, SECOND PARAGRAPH

The Examiner has rejected claims 8, 10 and 19 under 35 U.S.C. § 112, second paragraph, as being indefinite for a failing to recite the names of the claimed compounds which are found in Table 1 of the specification in the claims themselves. In response, Applicants have explicitly recited the compounds in Table 1 in each of claims 8, 10 and 19. As such, Applicants respectfully request that the rejection under 35 U.S.C. § 112, second paragraph be withdrawn.

V. REJECTION UNDER 35 U.S.C. § 103(a)

The Examiner has rejected claims 1-4 and 8-19 under 35 U.S.C. § 103(a) as allegedly being obvious over WO 00/48993 ("Altmann *et al.*") in view of WO 02/070517 ("Oballa *et al.*"). The Examiner alleges that Altmanm *et al.* disclose generically overlapping arylaminoalkylamide compounds as cathepsin inhibitors and that the combined teaching of

Altmann *et al.* with Oballa *et al.* makes the claimed invention obvious. In response, Applicants respectfully traverse the rejection.

> As set forth in M.P.E.P. § 2143, "[t]o establish a *prima facie* case of obviousness, *three* basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991)."

All three elements set forth above must be present in order to establish a *prima facie* case of obviousness. Applicants assert that a *prima facie* case of obviousness has not been established, namely because there is no suggestion or motivation to modify the references.

There is No Suggestion or Motivation to Modify the References

Applicants state that there is simply no motivation or suggestion provided in the cited references to modify their teaching in the way the Examiner has contemplated. Obviousness can only be established by combining or modifying the teachings of the cited art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988); *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992).

Altmann *et al.* describe certain arylaminoalkylamide compounds that are selective inhibitors of the cysteine protease enzyme, cathepsin K. Oballa *et al.* describe compounds that are generally *non-selective* inhibitors of the cathepsins K, L, S and B (see, Abstract).

A skilled artisan would not be motivated to combine the teachings of the cited art to arrive at the claimed invention as there is no teaching or suggestion to do so. As stated above, the present invention describes novel compounds that are *selective inhibitors of cathepsin S.* In clear contrast, Altmann *et al.* describe compounds that are selective inhibitors for *cathepsin K.* The lack of a teaching or suggestion in Altmann *et al.* for *selective* cathepsin S inhibitors is not

supplemented by the teaching of Oballa *et al.*, as Oballa *et al.* simply describe in general terms compounds that are *non-selective* inhibitors of many cathepsins enzymes, e.g., cathepsins K, L, S and B (see, Abstract). Oballa *et al.* do not teach or suggest compounds that are *selective* inhibitors of cathepsin S.

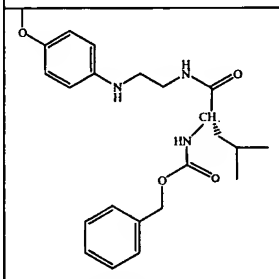
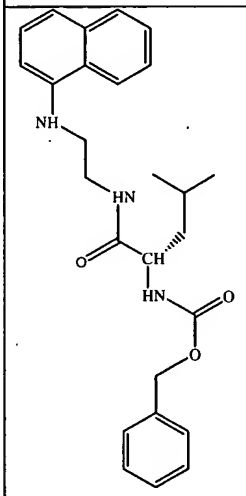
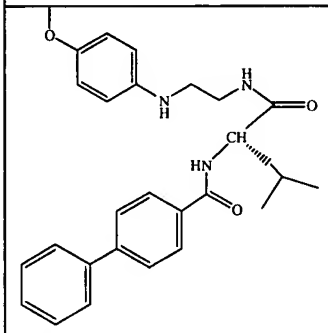
Applicants submit that there is simply no suggestion or motivation found in the cited references for making *selective* cathepsin S inhibitors as is presently taught and claimed. As such, a *prima facie* obviousness rejection has not been established. In view of the above, Applicants respectfully request that the obviousness rejection be withdrawn.

OBJECTIVE EVIDENCE REBUTS ANY *PRIMA FACIE* CASE OF OBVIOUSNESS

Applicants can rebut a *prima facie* case of obviousness by presenting comparative test data showing that the claimed invention possesses unexpectedly improved properties or properties that the prior art does not possess. *In re Dillion*, 16 U.S.P.Q. 1897, 1901 (Fed. Cir. 1990).

Applicants maintain that a *prima facie* case of obviousness has not been established. However, the comparative data filed with the application rebuts any *prima facie* case of obviousness. The Examiner's attention is respectfully directed to the table on page 125 of the present application which is reproduced below for the Examiner's convenience. As disclosed therein, a representative set of compounds disclosed in Altmann *et al.*, *i.e.*, compounds 14, 19 and 27, were tested by Applicants to evaluate their selectivity for the inhibition of cathepsin S over cathepsin K. Compounds 14, 19 and 27 appear on pages 25, 27 and 33, respectively, of Altmann *et al.*

Table on page 125 of the instant application:

Compound	Ki (CatS)[a] μM	Ki (CatK)[b] μM	Selectivity for Cat. S over Cat. K[c]
	++	+++	<10
	++	+++	<10
	+++	+++	<10

[a] Cathepsin S inhibition constant for the compounds +, <10 μM; ++, <1.0 μM; +++, <0.1 μM.
[a] Cathepsin K inhibition constant for the compounds +, <10 μM; ++, <1.0 μM; +++, <0.1 μM.
[c] Selectivity of the compounds for cathepsin S over cathepsin K: <10

The compounds of Altmann *et al.*, as represented in the above table, are *less than* 10-fold selective for inhibition of cathepsin S over cathepsin K. The above table clearly

demonstrates that the compounds encompassed by formula I of Altmann *et al.* show little, if any, selectivity for the inhibition of cathepsin S over cathepsin K.

In stark contrast, the compounds of the present invention which are embodied by Applicants' formula I show the superior unexpected property of selective cathepsin S inhibition over other isozymes in the cathepsin family. (see Table 2, on page 118, of the instant application for a comparison of cathepsins S to K activity for a representative set of compounds of the invention). Most of the compounds set forth in Table 2 show at least *100-fold greater selectivity* for cathepsin S over cathepsin K; certain compounds show over *1000-fold selectivity.* At the very least, all the compounds are more than 10-fold selective for cathepsin S over cathepsin K. The compounds of the present invention are unexpectedly *far more selective* in inhibiting cathepsin S over cathepsin K, compared to the compounds of Altmann *et al.*

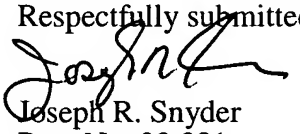
Thus, the compounds of formula I of the present application are *unexpectedly superior* in selectively inhibiting cathepsin S. This unexpected advantageous property represents objective evidence sufficient to rebut a *prima facie* case of obviousness. Accordingly, the Examiner is respectfully requested to withdraw the 35 U.S.C. § 103(a) rejection.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 925-472-5000.

Respectfully submitted,



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